



(51) International Patent Classification:

A61K 36/8962 (2006.01) *A61L 15/24* (2006.01)
A61K 9/00 (2006.01) *A61L 15/44* (2006.01)
A61K 47/32 (2006.01) *A61L 15/58* (2006.01)
A61K 9/70 (2006.01)

(21) International Application Number:

PCT/EP2013/076584

(22) International Filing Date:

13 December 2013 (13.12.2013)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/737,315 14 December 2012 (14.12.2012) US

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(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,
OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA,
SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: PATCH COMPRISING AN ONION EXTRACT

(57) Abstract: The present invention relates to a patch comprising a layer composition, wherein the layer composition comprises at least a backing liner, a matrix layer comprising an onion extract (A), an acrylate based polymer (B) or a thermoplastic hot melt adhesive (B*), and a release liner, wherein the matrix layer is disposed between the backing liner and the release liner such that the matrix layer is contacted by the backing liner and the release liner on opposite sides thereof, wherein the release liner is releasable from the matrix layer. Further the present invention relates to such a patch for use in treating and/or preventing scars.



WO 2014/091007 A1

Patch comprising an onion extract

The present invention relates to a patch comprising a layer composition, wherein the layer composition comprises at least a backing liner, a matrix layer comprising an onion extract (A), an acrylate based polymer (B) or a thermoplastic hot melt adhesive (B*), and a release liner, wherein the matrix layer is disposed between the backing liner and the release liner such that the matrix layer is contacted by the backing liner and the release liner on opposite sides thereof, wherein the release liner is releasable from the matrix layer. Further the present invention relates to such a patch for use in treating and/or preventing scars.

Scars are areas of fibrous tissue that replace normal skin after injury. A scar results from the biological process of wound healing in the skin and other tissues of the body. With the exception of very minor lesions, every wound (e.g. after accident, disease, or surgery) results in some degree of scarring.

Thus, a scar is an end product of a wound healing process. This end product is neither aesthetically nor functionally perfect. Unwounded dermis comprises a mechanically efficient meshwork of collagen. However, wound healing in human skin results in varying degrees of scar formation, ranging clinically from fine asymptomatic scars to problematic hypertrophic and keloid scars, which may limit function, restrict further growth. In addition they may have a poor cosmetic appearance.

Treatment options for scars range from invasive procedures and surgery such as excision or laser therapy to non-invasive management such as the application of pressure and, in particular, treatments with administration of topical agents. Moreover, scars frequently remain untreated.

Agents for treating scars are known in the art.

For example, the product Kelofibrase® is known as scar cream which comprises, as active ingredients, urea and heparin sodium (60 000 I.U.), and camphor as well as customary oil/emulsifier components. This product is reportedly useful for scar treatment, for scar contractures and keloids. Here, heparin-sodium acts, as is known, as a blood-thinning agent.

Under the name Hirudoid® forte is known a gel which comprises, as active ingredient, mucopolysaccharide polysulfuric ester (445 mg, corresponding to 40 000 units in 100 g of gel). Further ingredients are the components required for the preparation of the gel, such as

isopropyl alcohol, polyacrylic acid, propylene glycol and water. Mucopolysaccharide polysulfuric esters generally have a heparinoid effect and therefore correspond to the Kelofibrase® product specified above. As well as the gel, a Hirudoid® forte ointment is also known which, as well as the abovementioned active ingredients, has a mixture of monoglycerides and diglycerides with higher fatty acids and medium-chain triglycerides etc., and isopropyl alcohol, imide urea, phenoxyethanol and water. Products of this type can be used for treatment in cases of phlebopathies, superficial phlebitides, hematomas and for loosening hard scars. The product must not be applied to damaged skin.

Under the name Hylaform® is known a gel implant which contains crosslinked hyaluronic acid which is present in an aqueous sodium-chloride-containing solution for the purpose of injection. Using such an agent, skin deformations are said to be treatable. However, acute or chronic skin disorders in the affected correction area must not be present.

Under the name Linoladiol® N is known a hydrophilic O/W cream which comprises estradiol as active ingredient in the cream base. By means of this hormone-containing preparation, as well as gynecological applications, dermatological applications, such as burns, scar treatment, atrophy of the skin, perioral dermatitis and eczema in the acute and subacute stage are also stated. In this connection, however, the application limitations known for hormone-containing products, such as side effects and/or interactions, are to be taken into consideration to a considerable degree.

Further, some products for use in treating or preventing scar formation which comprise plant extracts as active ingredients are described.

In particular, gel-like products are used for this purpose. U.S. Pat. No. 5,885,581 describes such a gel-like product which comprises 20-30% by weight of polyethylene glycol 200, 0.005-0.03% by weight of preservative, 0.05-0.2% by weight of sorbic acid, 0.5-2% by weight of allantoin, 1-3% by weight of xanthan and, if desired, perfume substances, and which is characterized by 5-15% by weight of a liquid onion extract (*Allium cepa* extract), based on an aqueous carrier in an amount of about 55-65% by weight. The product thus represents a fat- (oil) -free gel and is applied externally to damaged skin tissue, in particular scarred tissue. The product is further characterized by a pH of 4.5-5.5 and a particle size of less than 50 nm.

Under the product name Contractubex®, a gel is known which comprises an onion extract (*Allium cepa* extract). Onion extracts for the treatment of scars are also disclosed in US 2010/0247689.

The product name PC 30 V describes a liquidum which comprises horse chestnut seed dry extract and also camomile blossom dry extract in 1,3-butanediol, dexpanthenol, allantoin and odor substances. This agent is said to be useful in the treatment of skin damage, such as wound chafing of sensitive pressure points and scars by orthopedic apparatuses, and also pressure sores. An indication with regard to scars as a result of operations or other skin damage is not stated here.

WO 2011/006100 discloses corticosteroids for reducing scar formation.

DE-A 37 23 248 relates to the use of thiosulfinic acid derivatives for the treatment of inflammations. These may be obtained, inter alia, by extraction from onions and subsequent chromatography. Onion extract itself is not used here.

EP-B 429 080 relates to a preparation process for S-allylcysteine-containing products, where, for example, aqueous garlic extracts are admixed with cysteine, giving S-allylcysteine.

EP-B 364 442 relates to an oil extract from at least 3 different herbs chosen from *Euphorbia*, veronica, yarrow, fumitory, garlic, nettle and marigold. This combination is used in the form of an oil, e.g. with paraffin, against psoriasis.

EP-B EP 201 956 relates to the extraction and chromatographic fractionation of, for example, tobacco, algae, garlic, where the specific substances obtained are reportedly useful for cosmetic or therapeutic applications.

The use of pressure dressings is further known for scar treatment. Application of pressure apparently increases the activity of collagenase, which is an enzyme capable of degrading and modeling the scar tissue and is employed by the body in the equilibrium of the formation and degradation of collagen during the healing process. However, pressure dressings are often very bulky rendering them uncomfortable to the user and often inconvenient to keep in place on the affected scar tissue.

Besides, it has been discovered in recent years that the shrinkage of hypertrophic scars can be increased by applying silicone-gel plates or sheets to the scars. The exact mechanism by which the silicone-gel interacts with such scars has not been established, however. A number of products are available commercially for this purpose, for instance such products as Dow Corning Silastic Sheeting, Cica-Care (Smith & Nephew), Epi-Derm (Biodermis), Nagosil (Nagor), among others. These products have the form of molded silicone-gel sheets having a thickness of 2-4 millimeters. In treating hypertrophic scars, these sheets are placed over the scars and are worn for a relatively long period of time, often from 3-12

months, until the scars either have decreased or have regenerated. Examples of recent patents which disclose such silicone-gel sheets include U.S. Pat. Nos. 5,759,560; 5,891,076; 5,895,656 and 5,919,476. The known silicone sheets are relatively rigid and after having been placed over the scar have insufficient adhesion to remain securely in position without some form of assistance. Consequently, it is necessary to secure the sheets against the skin with the aid of securing stocking, bandage, self-adhesive tape or some like means. The sheets often trap too much moisture causing irritation on the affected area. Additionally, gel sheets of the type that utilize silicone are tacky to the touch, both on the inner body, body contacting surface and the exterior surface. Having a body contacting surface which is tacky to the touch is advantageous and desirable. However, having an exterior which is tacky to the touch is not. A disadvantage of having a tacky exterior is that articles of clothing tend to adhere to the gel sheet. This presents several problems. One problem is that often the gel sheet adheres to an article of clothing with greater force than it adheres to the skin. Thus, when the article of clothing is removed, the gel sheet is removed from the body. Another problem is that the articles of clothing would adhere to the gel sheet and prevent normal range of motion. An additional problem encountered with gel sheets which are tacky to the touch is that they tend to become soiled more quickly.

Further active substance patches have been described in the prior art, some of which operate in accordance with the reservoir principle, where the active substance is delivered, for example, by way of a matrix system or with a relatively complex multilayer structure. In particular hot melt self-adhesive compositions have been proposed for this purpose, as for example in EP-A 663 431, EP-A 452 034, EP-A 305 757, DE-A43 10 012, DE-A 42 22 334 and DE-C 42 24 325. However, in the hot melt process, active substances may decompose due to the high temperature applied in this process. Further, no patches comprising a plant extract for scar treatment were described.

The other physical treatments for scars available including surgery, X-ray therapy and cryotherapy are expensive or potentially dangerous and not normally recommended. Accordingly, while there have been physical treatments, these treatments are expensive, inconvenient to use, difficult to apply or simply have not been very effective in achieving the desired purpose.

Thus, there remains the need for advantageous agents for scar treatment.

SUMMARY OF THE INVENTION

The present invention relates to a patch comprising a layer composition, wherein the layer composition comprises at least a backing liner, a matrix layer comprising an onion extract (A), an acrylate based polymer (B) or a thermoplastic hot melt adhesive (B*), and a release

liner, wherein the matrix layer is disposed between the backing liner and the release liner such that the matrix layer is contacted by the backing liner and the release liner on opposite sides thereof, wherein the release liner is releasable from the matrix layer.

The present invention further relates to a method for manufacturing a patch comprising a layer composition, wherein the layer composition comprises at least a backing liner, a matrix layer comprising an onion extract (A), an acrylate based polymer (B) or a thermoplastic hot melt adhesive (B*), and a release liner, wherein the matrix layer is disposed between the backing liner and the release liner such that the matrix layer is contacted by the backing liner and the release liner on opposite sides thereof, wherein the release liner is releasable from the matrix layer, wherein the method comprises the following steps:

- (a) providing the release liner,
- (b) applying a coating mass comprising an onion extract (A*) and
 - an acrylate based polymer (B), or
 - a thermoplastic hot melt adhesive composition (B**)to the release liner,
- (c) drying the release liner and the coating mass applied thereto such that the matrix layer is formed on the release layer, said matrix layer comprising an onion extract (A) and
 - an acrylate based polymer (B), or
 - a thermoplastic hot melt adhesive (B*)
- (d) and covering the matrix layer by means of the backing liner.

Further, the present invention relates to a patch obtained or obtainable by the method described above as well as to a patch, as described above, for use in treating and/or preventing a scar.

Furthermore, the present invention relates to a method for treating and/or preventing scars in a subject in need thereof comprising applying to said subject a patch, as described above.

DETAILED DESCRIPTION

It has surprisingly been found that the patch, described hereinabove and below, is convenient to use, easy to apply to a subject in need thereof, remains secure in position on the subject, has good pressure sensitive adhesive properties and releases the active ingredient, i.e. the onion extract, in a controlled manner. In particular, it has been found that the patch according to the invention containing at least the onion extract as active

substance displays a high level of efficacy, i.e. a relatively high rate of release, as well as a good skin compatibility coupled with good adhesion. Further, the removal is easy and without inducing any irritation to the skin of the subject or any pain. Further, the patch may be prepared in a safe manner while avoiding any decomposition of the onion extract.

- 5 Therefore, in a first aspect, the present invention concerns a patch comprising a layer composition, wherein the layer composition comprises at least a backing liner, a matrix layer comprising an onion extract (A), an acrylate based polymer (B) or a thermoplastic hot melt adhesive (B*), and a release liner, wherein the matrix layer is disposed between the backing liner and the release liner such that the matrix layer is contacted by the backing
10 liner and the release liner on opposite sides thereof, wherein the release liner is releasable from the matrix layer.

The matrix layer:

As described above, the matrix layer comprises an onion extract (A) and an acrylate based polymer (B), or an onion extract (A) and a thermoplastic hot melt adhesive (B*).

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The Onion extract (A)

- As used herein, the term "onion" refers to any *Allium* species including, but not limited to, *Allium cepa*, *Allium fistulosum*, *Allium schoenoprasum*, *Allium ascalonicum*, *Allium*
20 *cernuum*, and *Allium ampeloprasum*. Thus, as used herein, the term "onion" means any type of onion including, but not limited to, any cultivated onion, any wild onion, any onion species, any intra- and inter-species onion crosses, all onion varieties, all onion genotypes and all onion cultivars.

Preferably, the extracts are obtained from the bulbs of the onion.

- 25 In particular, the onion extract (A) is an *Allium cepa* extract.

Thus, the present invention also relates to a patch, as described above, wherein the onion extract (A) is an *Allium cepa* extract. Likewise, the present invention relates to a method for preparing a patch, as described above, and a patch obtainable or obtained by said method, wherein the onion extract (A) is an *Allium cepa* extract.

- 30 Preferably, the amount of the onion extract (A), more preferably the *Allium cepa* extract (A), present in the matrix layer according to the invention is in the range of from 0.01 to 5 % by weight, more preferably in the range of from 0.02 to 4 % by weight, more

preferably in the range of from 0.1 to 3 % by weight, more preferably in the range of from 0.3 to 2 % by weight, more preferably in the range of from 0.5 to 1.5 % by weight, and most preferably in the range of from 0.9 to 1.1 % by weight, such as preferably 1.0 % by weight, based on the total weight of the matrix layer.

- 5 The term "onion extract (A)" as used herein means a substance or composition obtained from an onion by a process comprising the extraction, maceration or percolation of the onion material. The onion extract (A) which is present in the matrix layer refers to dry onion extract which is obtained by evaporation of the whole liquid extract to dryness. Thus, the term "onion extract" refers to all onion components present in the liquid extract
- 10 (A*) which is obtained by the process comprising the extraction, maceration or percolation of the onion material which are not removed in the evaporation process together with the respective solvent. The term "evaporation of the whole liquid extract to dryness" in this context is denoted to mean that at least 99 % by weight, more preferably at least 99.9 % by weight, preferably all of the solvent being present in the onion extract (A*) obtained by the
- 15 process comprising the extraction, maceration or percolation of the onion material as described above is removed to give the onion extract (A). Solvents suitable for extraction, percolation or maceration are known to those experienced in the art. Acetone, chloroform, ethyl acetate, lower alkanols with 1 to 4 carbon atoms, alcohols or a mixture of these and water are particularly suited. Carbon dioxide in fluid or super-critical form and pressurized
- 20 gases with solvent properties are also suitable as extraction agents.

Preferably the onion extract (A*) comprises a solvent S₂, wherein said solvent is either the solvent used for extraction, maceration or percolation of the onion material or a solvent used for redissolving the dry extract.

- 25 Preferably, S₂ comprises at least one alcohol and water. As to the at least one alcohol, this alcohol is preferably selected from the group consisting of ethanol, propanol, iso-propanol or mixtures thereof. Most preferably, the at least one alcohol is ethanol.

- In particular, the solvent S₂ comprises water in an amount in the range of from 95 to 75 % by weight, preferably in the range of from 90 to 84 % by weight, and most preferably in the range of from 92 to 82 % by weight, based on the total weight of the solvent S₂. As
- 30 described above, the solvent S₂ comprises the at least one alcohol, wherein said at least one alcohol is preferably present in the range of from 5 to 25 % by weight, preferably in the range of from 8 to 18 % by weight, and most preferably in the range of from 10 to 16 % by weight, based on the total weight of the solvent S₂.

- Preferably S₂ comprises ethanol in an amount in the range of from 5 to 25 % by weight and
- 35 water in an amount of from 95 to 75 % by weight, more preferably ethanol in an amount in

the range of from 8 to 18 % by weight and water in an amount of from 92 to 82 % by weight, and most preferably ethanol in an amount in the range of from 10 to 16 % by weight and water in an amount of from 90 to 84 % by weight.

Thus, the present invention also relates to a method for manufacturing a patch, as described
5 above, as well as to a patch obtained or obtainable by said method, wherein the onion extract (A*) comprises a solvent S₂, wherein S₂ comprises ethanol in an amount in the range of from 5 to 25 % by weight and water in an amount of from 95 to 75 % by weight, based on the total weight of the solvent S₂.

S₂ may optionally comprise further organic solvents such as, for example, isopropanol or
10 methanol. Preferably, S₂ comprises less than 0.1 % by weight of further organic solvents in total, preferably less than 0.05 % by weight, based on the total weight of the solvent S₂. As to the amount of onion components present in the onion extract, these components are preferably present in an amount of 20 to 33 % by weight, preferably 25 to 30 by weight, based on the total amount the onion extract (A*), wherein this amount refers to the weight
15 of the dry onion extract, before dissolving this dry onion extract in the Solvent S₂.

According to a preferred embodiment of the invention, the onion extract (A*) is an onion
extract which is obtained or obtainable by a process comprising an extraction, maceration or percolation of the onion material, either of fresh or dried onions, with a suitable solvent S₁ and a subsequent partial or preferably complete removal of the solvent. Preferably, after
20 complete removal of the solvent, the remaining residue is redissolved in at least one suitable solvent, preferably in the above described solvent S₂. Optionally, the process for preparing the onion extract (A*) may comprise further steps, such as purification steps, in particular filtration steps.

As to the solvent used in the process to obtain the onion extract described above, any
25 suitable solvent may be used. This solvent is referred to hereinunder as solvent S₁. S₁ may be the same or may differ from the above described solvent S₂. Preferably, S₁ comprises at least one alcohol. As to the at least one alcohol, this alcohol is preferably selected from the group consisting of ethanol, propanol, iso-propanol or mixtures thereof. Most preferably, the at least one alcohol comprised in S₁ is ethanol.

30 Preferably, the at least one alcohol is present in an amount of at least 70 % by weight, preferably of at least 80 % by weight, more preferably of at least 90 % by weight, and most preferably of at least 96 % by weight, based on the total weight of the solvent S₁.

S₁ may optionally comprise water and/or further organic solvents such as, for example, isopropanol or methanol. Preferably, S₁ comprises less than 0.1 % by weight of further
35 organic solvents in total, preferably less than 0.05 % by weight based on the total weight of

the solvent S_1 . In particular, S_1 comprises water in an amount of less than 30 % by weight, preferably of less than 20 % by weight, more preferably of less than 10 % by weight, and most preferably of less than 4 % by weight.

5 According to an alternative embodiment of the invention, S_1 comprises ethanol in an amount in the range of from 5 to 25 % by weight and water in an amount of from 95 to 75 % by weight, more preferably ethanol in an amount in the range of from 8 to 18 % by weight and water in an amount of from 92 to 82 % by weight, and most preferably ethanol in an amount in the range of from 10 to 16 % by weight and water in an amount of from 90 to 84 % by weight.

10 Preferably, fresh or dried onions or parts of onions, such as onion chips, are extracted with a solvent S_1 , as described above, comprising at least one alcohol to give a liquid phase L_1 and a solid residue R_0 , or a composition consisting of the liquid phase L_1 and the solid residue R_0 .

15 In particular, the ratio of amount of onion (weight) to solvent S_1 (weight) is in the range of from 0.5 : 0.9 to 0.7 : 1, more preferably in the range of from about 0.65 : 1.

The extraction can be carried out in one or more extraction steps. Preferably a multi-stage extraction is carried out in which a multiplicity of separating stages connected in series is used.

20 After the extraction, described above, the liquid phase (L_1) is preferably separated from the solid residue (R_0).

Between the separation step and the extraction step, the liquid phase L_1 and the solid residue R_0 are preferably allowed to stand for a time in the range of from 1 h to 4 weeks, preferably in the range of from 1 day to 3 weeks, more preferably about 1 to 2 weeks, in particular at a temperature in the range of from 10 to 40 °C, more preferably at a
25 temperature in the range of from 10 to 30 °C, most preferably at room temperature. Thereby, further solid residue R_0 may precipitate from the liquid phase L_1 .

The separation step may be carried out by any suitable method known to those skilled in the art. According to one embodiment of the invention, the separation is carried out by filtration. The term "filtration" or "filtering" refers to the process of removing essentially
30 all, preferably all, of the solid residue R_0 , which may be present as suspended particles, from the liquid phase by passing the composition through one or more membranes or filters.

The liquid phase L_1 obtained is subsequently, optional after further purification steps, concentrated, preferably evaporated to dryness as mentioned above, to give residue R_1 .

Optionally, the liquid phase L_1 obtained is allowed to stand for a time in the range of from 1 h to 4 weeks, preferably in the range of from 1 day to 3 weeks, more preferably about 1 to 2 weeks, in particular at a temperature in the range of from 10 to 40 °C, more preferably at a temperature in the range of from 10 to 30 °C, most preferably at room temperature. Thereby, further solid residue may precipitate from the liquid phase L_1 . In case further precipitates are formed, preferably at least one filtration is carried out.

In the preferred case in which L_1 is evaporated to dryness, the residue R_1 corresponds to the dry onion extract mentioned above.

Subsequent to the evaporating step, the method may comprise further steps, such as, e.g. at least one purification step and/or at least one homogenization step. Preferably, the residue R_1 , more preferably the dry onion extract R_1 , is at least homogenized.

As described above, residue R_1 , preferably the homogenized residue R_1 , is preferably redissolved in the above-described solvent S_2 , with S_2 preferably comprising at least one alcohol and water, to give the onion extract (A^*).

Preferably, the onion extract (A^*) comprises the solvent S_2 in an amount in the range of from 67 to 80 % by weight, preferably in the range of from 70 to 75 % by weight, more preferably in the range of from 70 to 72 % by weight, based on the total weight of the onion extract (A). Further, the onion extract (A^*) preferably comprises the residue R_1 in an amount in the range of from 20 to 33 % by weight, preferably in the range of from 25 to 30 % by weight, more preferably in the range of from 28 to 30 % by weight, based on the total weight of the onion extract (A^*).

In particular, the onion extract (A^*) consists of 20 to 33 % by weight of residue R_1 and 67 to 80 % by weight of the solvent S_2 , preferably of 25 to 30 % by weight of residue R_1 and 70 to 75 % by weight of the solvent S_2 , and most preferably of 28 to 30 % by weight of residue R_1 and 70 to 72 % by weight of the solvent S_2 , based on the total amount of the onion extract (A^*), with the sum of the amounts of R_1 and S_2 giving 100 % by weight.

Preferably, the onion extract (A^*) is an onion extract obtained or obtainable by a process comprising the steps of

- (a1) extracting fresh or dried onions, preferably *Allium cepa*, with a solvent S_1 comprising at least one alcohol to give a liquid phase L_1 and a solid residue R_0 ,
- (b1) separating the liquid phase L_1 from the solid residue R_0 ,
- (c1) evaporating the liquid phase L_1 to give a residue R_1 ,
- (d1) redissolving the residue R_1 in a solvent S_2 comprising at least one alcohol and water to give an onion extract (A^*),

wherein the onion extract (A*) comprises R₁ preferably in an amount of 20 to 33 % by weight, based on the total weight of the onion extract (A*).

The onion extract (A*) is then preferably applied together with at least the acrylate based polymer or the thermoplastic hot melt adhesive composition (B**) onto the release liner,
 5 and the release liner and the coating mass applied thereto are dried such that the matrix layer comprising the onion extract (A) and the acrylate based polymer (B), or the onion extract (A) and the thermoplastic hot melt adhesive (B*), is formed on the release layer.

Thus, the present invention also relates to a method for manufacturing a patch and to a patch obtained or obtainable by said method, wherein the method comprises the following
 10 steps:

- (a) providing the release liner,
- (b) applying a coating mass comprising an onion extract (A*) and
 - an acrylate based polymer (B), or
 - a thermoplastic hot melt adhesive composition (B**)
 15 to the release liner,
- (c) drying the release liner and the coating mass applied thereto such that the matrix layer is formed on the release layer, said matrix layer comprising an onion extract (A) and
 - an acrylate based polymer (B), or
 - a thermoplastic hot melt adhesive (B*)
 20

and covering the matrix layer by means of the backing liner, wherein the onion extract (A*) is an onion extract obtained or obtainable by a process comprising the steps

- (a1) extracting fresh or dried onions, preferably *Allium cepa*, with a solvent S₁ comprising at least one alcohol to give a liquid phase L₁ and a solid residue R₀,
 25
- (b1) separating the liquid phase L₁ from the solid residue R₀,
- (c1) evaporating the liquid phase L₁ to give a residue R₁,
- (d1) redissolving the residue R₁ in a solvent S₂ comprising at least one alcohol and water to give an onion extract (A*)

The Polyacrylate Polymer

As described above, according to one embodiment of the invention, the matrix layer comprises the polymer (B), said polymer being an acrylate based polymer. The term "acrylate based polymer" refers to polymers comprising building blocks derived from
 35 acrylate monomers, thus monomers of the formula CH₂=CH-COOR. Typical acrylate

monomers are normally alkyl acrylates with R being an alkyl group, in particular an alkyl group having of from 1 to 20 carbon atoms, preferably 4 to 10 carbons. Useful alkyl acrylates include ethyl acrylate, butyl acrylate, amyl acrylate, hexyl acrylate, 2-ethylhexyl acrylate, ethylhexyl acrylate, octyl acrylate, isooctyl acrylate, decyl acrylate, dodecyl acrylates, with 2-ethylhexyl acrylate, butyl acrylate, and iso-octyl acrylate being preferred.

Preferably the acrylate based polymer is an acrylate-vinylacetate based polymer. The term "acrylate-vinylacetate based polymer" refers to co-polymers comprising building blocks derived from the monomeric components acrylate (B1) and vinylacetate (B2).

Thus, the present invention also relates to a patch, as described above, and a patch obtainable or obtained by the above described method, wherein the matrix layer comprises acrylate-vinylacetate based polymer (B) comprising building blocks derived from the monomeric components acrylate (B1) and vinylacetate (B2). Preferably the acrylate (B1) is selected from the group consisting of 2-ethylhexyl acrylate, ethylhexyl acrylate butylacrylate or a mixture of two or more thereof.

The polymer (B) may comprise further building blocks besides the building blocks derived from acrylate (B1) and optionally vinylacetate. According to one preferred embodiment of the invention, the polymer (B) further comprises building blocks derived from acrylamides, in particular derived from t-octyl acrylamid.

Preferably, the polymer (B) further comprises building blocks derived from functional monomers which, when incorporated into the polymer (B), result in building blocks comprising carboxylic acid groups. Useful carboxylic acid monomers to provide the functional group preferably contain from about 3 to about 6 carbon atoms and include, among others, acrylic acid, methacrylic acid, itaconic acid and the like. Acrylic acid, methacrylic acid and mixtures thereof are preferred as acids. In particular, the polymer comprises acrylic acid.

According to a particularly preferred embodiment, the polymer (B) comprises, preferably essentially consists of, building blocks derived from acrylic acid, 2-ethylhexyl acrylate and vinyl acetate.

According to a further preferred embodiment, the polymer (B) comprises, preferably essentially consist of, building blocks derived from acrylic acid, ethylhexyl acrylate, butyl acrylate, t-octylacrylamide and vinyl acetate.

Preferably, the polymer (B) comprises a crosslinking agent, such as an external crosslinking agent and/or an internal crosslinking agent.

The term "internal crosslinking agent" is denoted to mean building blocks derived from polyfunctional monomers, which when incorporated into the polymer during polymerization as building block form act as crosslinker. As example, compounds having at least two non-conjugated carbon-carbon double bonds per molecule are mentioned, in particular diallyl maleate, diallyl phthalate and multifunctional acrylates and methacrylates including polyethylene glycol diacrylate, hexanediol diacrylate, ethoxylated trimethylolpropane triacrylate, pentaerythritol triacrylate, propylene glycol diacrylate and trimethylolpropane trimethacrylate.

The term "external crosslinking agent" is denoted to mean a compound which causes post polymerization crosslinking. External crosslinking agents include metal salts such as zirconium ammonium carbonate, zinc ammonium carbonate, aluminum acetate, zinc acetate and chromium acetate.

Preferably, the matrix layer comprises the acrylate based polymer (B) in an amount in the range of from 99.8 to 80 % by weight, more preferably in the range of from 99.5 to 84 % by weight, more preferably in the range of from 98.8 to 89 % by weight, more preferably in the range of from 98.4 to 92 % by weight, more preferably in the range of from 97.5 to 93,5 % by weight, and most preferably in the range of from 96 to 94 % by weight, such as preferably 95 % by weight, based on the total weight of the matrix layer.

The thermoplastic hot melt adhesive composition B** and the thermoplastic hot melt adhesive B*.

As described above, according to another embodiment of the invention, the matrix layer comprises the hot melt adhesive (B*), wherein said matrix layer is preferably obtained or obtainable by applying a coating mass comprising an onion extract (A*) and a thermoplastic hot melt adhesive composition (B**) to the release liner, and drying the release liner and the coating mass applied thereto such that the matrix layer is formed on the release layer, said matrix layer comprising an onion extract (A) and the thermoplastic hot melt adhesive (B*)

The term "thermoplastic" refers to the capability of a compound to reversibly soften or fuse when heated and harden again when cooled. Hot melt adhesives are solid adhesives which can be applied as a melt to the substrates to be joined and harden by solidification during cooling after assembly at room temperature. In thermoplastic adhesives, this process is reversible. It is based essentially on material characteristics attributable to polymers such as polyamides, polyesters, polystyrenes or polyolefins. These polymers decisively determine the adhesive properties regarding adhesion, strength and temperature characteristics. To increase adhesion usually tackifiers are added. Further, these hot melt

adhesives usually comprise plasticizers to enhance flexibility and/or waxes and/or crystallization accelerators to improve the morphology. The properties of the hot melt materials can also be selectively changed by addition of similar or different polymers.

Usually the molten adhesive is sprayed, or coated as a film. Typically hot melt adhesives
5 can be based on polymers such as polyolefins (ethylene- or propene-based polymers), or functionalized polyolefins (ethylene or propene copolymers with oxygenated function containing monomers), or styrene block copolymers containing at least one rubbery phase, like SIS, or SBS. Styrene block copolymers are of interest due to their dual characteristics, i.e. cohesion of the styrenic phase associated with the rubber behavior of another phase.

10 Preferably, the polymer (B*) is a hot melt thermoplastic rubber. Preferably, the hot melt adhesive composition (B**) and the hot melt adhesive (B*) comprise a styrene polymer, more preferably a styrene block co-polymer such as SIS or SBS.

Thus, the present invention also relates to a patch, as described above, wherein the matrix layer comprises a hot melt adhesive (B*), wherein said hot melt adhesive comprise a
15 styrene polymer, more preferably a styrene block co-polymer. Further, the present invention relates to a method, as described above, comprising applying a coating mass comprising an onion extract (A*) and a thermoplastic hot melt adhesive composition (B**) to the release liner, and drying the release liner and the coating mass applied thereto such that the matrix layer is formed on the release layer, said matrix layer comprising an onion
20 extract (A) and the thermoplastic hot melt adhesive (B*), the hot melt adhesive composition (B**) and the hot melt adhesive (B*) comprise a styrene polymer, more preferably a styrene block co-polymer.

More preferably, the hot melt adhesive composition (B**) and the hot melt adhesive (B*) additionally comprise at least one tackifying resin and/or at least one plasticizer.

25 The tackifying resin is preferably selected from the group consisting of aliphatic hydrocarbon resins and their hydrogenated derivatives, hydrogenated cycloaliphatic hydrocarbon resins, aromatic modified aliphatic or hydrogenated cycloaliphatic hydrocarbon resins, aliphatic modified aromatic hydrocarbon resins, partially or fully hydrogenated aromatic hydrocarbon resins, polyterpene, terpene-phenol resins,
30 hydrogenated resin ester and styrenated polyterpene resins.

A suitable plasticizer may be selected from the group, which not only includes the usual plasticizing oils such as mineral oil but also olefin oligomers and low molecular weight polymers, glycol benzoates, as well as vegetable and animal oil and derivatives of such oils. The oligomers may be polypropylenes, liquid polybutenes, hydrogenated
35 polyisoprene, hydrogenated butadiene or the like having average molecular weights

between about 100 and about 10,000 g/mol. Suitable vegetable and animal oils include glycerol esters of the usual fatty acids and polymerization products thereof. Other plasticizers may be used provided they have suitable compatibility.

Further, the the hot melt adhesive composition B** and the hot melt adhesive B* preferably comprise additionally at least one stabilizer or antioxidant. Examples include sterically hindered phenols, phosphites or thioesters, high molecular weight hindered phenols and multifunctional phenols such as sulfur and phosphorus-containing phenols. Hindered phenols are well known to those skilled in the art and may be characterized as phenolic compounds which also contain sterically bulky radicals in close proximity to the phenolic hydroxyl group thereof. In particular, tertiary butyl groups generally are substituted onto the benzene ring in at least one of the ortho positions relative to the phenolic hydroxy group. The presence of these sterically bulky substituted radicals in the vicinity of the hydroxyl group serves to regard its stretching frequency and, correspondingly, its reactivity; this steric hindrance thus providing the phenolic compound with its stabilizing properties. Representative hindered phenols include; 1,3,5-trimethyl 2,4,6-tris(3,5-di-tert-butyl-4-hydroxybenzyl) benzene; pentaerythrityl tetrakis-3 (3,5-di-tert-butyl-4-hydroxyphenyl) propionate; n-octadecyl-3 3,5-di-tert-butyl-4-hydroxyphenyl)-propionate; 4,4'-methylenebis (2,6-tert-butylphenol); 4,4'-thiobis (6-tert-butyl-o-cresol); 2,6-di-tertbutylphenol; 6-(4-hydroxyphenoxy)-2,4-bis(n-octyl-thio)1,3,5 triazine; di-n-octadecyl 3,5-di-tert-butyl-4-hydroxy-benzylphosphonate; 2-(n-octylthio) ethyl 3,5-di-tert-butyl-4-hydroxy-benzoate; and sorbitol.

Further additives, such as colorants such as titanium dioxide, fillers such as talc, clay or adhesion promoters may be present. Such additives are usually used in amounts of up to 5 wt.-%, preferably in amounts of from about 3 to 5 wt.-% of the hot melt adhesive. Suitable additives are known to the expert.

Suitable hot melt adhesive compositions are, e.g., Nolax M11.13, Nolax M13.320, Dermatak H447A and Dermatak H524B.

Preferably, the matrix layer comprising the thermoplastic hot melt adhesive (B*), and the onion extract (A) is obtained, by

- (a2) dissolving a thermoplastic hot melt adhesive composition (B**) in a solvent S^{hm},
- (b2) mixing this solution with at least an onion extract (A*) to give a coating mass,
- (c2) applying the coating mass onto a release liner, and

drying the release liner and the coating mass applied thereto such that the matrix layer comprising an onion extract (A) and the thermoplastic hot melt adhesive (B*) is formed on the release layer.

5 Preferably step (c2) is carried out at a temperature in the range of from 0 to 50 °C, more preferably, in the range of from 5 to 40 °C, more preferably at a temperature in the range of from 10 to 30 °C, more preferably at a temperature in the range of from 15 to 25 °C.

10 Surprisingly, it has been found that a suitable matrix comprising an onion extract may be prepared without melting the adhesive prior to its application onto the release liner but instead by dissolving or dispersing a hot melt adhesive composition in a solvent to give a coating mass and by applying this coating mass onto the release liner. This process is particularly advantageous in that the onion extract is stable under these conditions so that any decomposition of the onion extract due to too high temperatures may be avoided. Thus, preferably the thermoplastic hot melt adhesive composition B** is not melted in order to apply the coating mass onto the release liner. Instead, the thermoplastic hot melt
15 adhesive composition B** is dissolved or dispersed in a solvent and the solution or dispersion is applied onto the release liner.

Thus, the present invention also relates to a patch comprising a layer composition, wherein the layer composition comprises at least

- 20 a) a backing liner,
- b) a matrix layer comprising an onion extract (A), and
 - an acrylate based polymer (B), or
 - a thermoplastic hot melt adhesive (B*),
- c) and a release liner, wherein

25 the matrix layer is disposed between the backing liner and the release liner such that the matrix layer is contacted by the backing liner and the release liner on opposite sides thereof, wherein the release liner is releasable from the matrix layer, and wherein in case the matrix layer comprises a thermoplastic hot melt adhesive (B*), and an onion extract (A), wherein the matrix layer is obtained, by

- 30 - dissolving or dispersing a thermoplastic hot melt adhesive composition (B**) in a solvent S^{hm} ,
- mixing this solution or dispersion with at least an onion extract (A*) to give a coating mass,
- applying the coating mass onto a release liner, and

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- drying the release liner and the coating mass applied thereto such that the matrix layer comprising an onion extract (A) and the thermoplastic hot melt adhesive (B*) is formed on the release layer, and comprising an onion extract (A*) and an thermoplastic hot melt adhesive (B*) to the release liner,
- 5 preferably wherein the hot melt adhesive composition B** is not melted prior to the application of the coating mass onto the release liner.

The solvent S^{bm} is preferably an organic solvent, more preferably an organic solvent selected from the group consisting of hexane, cyclohexane, toluene, methylethylketone, ethyl acetate, heptane and mixtures of two or more thereof, more preferably ethyl acetate
 10 and/or heptane.

Emulsifier:

Preferably, the matrix layer comprises at least one emulsifier. In particular, the at least one
 15 emulsifier (i.e., emulsifying agents) is preferably used in amounts effective to provide uniform blending of ingredients present in the coating mass prior to applying said coating mass to the release liner.

Thus, the present invention also relates to a patch, as described above, and a patch
 20 obtainable or obtained by the above described method, wherein the matrix layer comprises at least one emulsifier.

Preferred emulsifiers include one or more of

- 25 (i) anionics such as fatty acid soaps, e.g., potassium stearate, sodium stearate, ammonium stearate, and triethanolamine stearate; polyol fatty acid monoesters containing fatty acid soaps, e.g., glycerol monostearate containing either potassium or sodium salt; sulfuric esters (sodium salts), e.g., sodium lauryl 5 sulfate, and sodium cetyl sulfate; and polyol fatty acid monoesters containing sulfuric esters, e.g., glyceryl monostearate
 30 containing sodium lauryl surfate; in particular
- (ii) cationics such as N(stearoyl colamino formylmethyl) pyridium; N-soya-N-ethyl morpholinium ethosulfate; alkyl dimethyl benzyl ammonium chloride; diisobutylphenoxythoxyethyl dimethyl benzyl ammonium chloride; and cetyl
 35 pyridium chloride; and

(iii) nonionics such as polyoxyethylene fatty alcohol ethers, e.g., monostearate; polyoxyethylene lauryl alcohol; polyoxypropylene fatty alcohol ethers, e.g., propoxylated oleyl alcohol; polyoxyethylene fatty acid esters, e.g., polyoxyethylene stearate; polyoxyethylene sorbitan fatty acid esters, e.g., polyoxyethylene sorbitan monostearate; sorbitan fatty acid esters, e.g., sorbitan; polyoxyethylene glycol fatty acid esters, e.g., polyoxyethylene glycol monostearate; and polyol fatty acid esters, e.g., glyceryl monostearate and propylene glycol monostearate; and ethoxylated lanolin derivatives, e.g., ethoxylated lanolins, ethoxylated lanolin alcohols and ethoxylated cholesterol, glyceryl monooleat and caprylocaproyl macrogol glyceride.

Preferably, the emulsifier is a nonionic surfactant, more preferably a surfactant selected from the group consisting of polyethyleneglycol hydroxystearate, such as polyethylene glycol (15)-hydroxystearate (such as Solutol®), glyceryl monooleate (Peceol®), a caprylocaproyl macrogol glyceride (Labrasol®), cremophor, and mixtures of two or more thereof.

Most preferably, the emulsifier is caprylocaproyl macrogol glyceride (Labrasol®).

Thus, the present invention also relates to a patch, as described above, and a patch obtainable or obtained by the above described method, wherein the matrix layer comprises caprylocaproyl macrogol glyceride as emulsifier.

Preferably, the matrix layer comprises the at least one emulsifier in an amount in the range of from 0.1 to 10 % by weight, more preferably in the range of from 0.5 to 8 % by weight, more preferably in the range of from 1 to 5 % by weight, more preferably in the range of from 1 to 4 % by weight, more preferably in the range of from 1.5 to 3.5 % by weight, and most preferably in an amount of about 3 % by weight, based on the total weight of the matrix layer.

Further active agents:

The matrix layer present in the patch of the present invention may also comprise, besides the onion extract (A), at least one further active agent, in particular agents that sooth, condition and/or heal the skin.

The contained active agent may be selected from all active agents and mixtures thereof that can be applied to the surface of the skin. The active agent can act cosmetically or pharmaceutically. The active agent can be completely of plant origin or can be synthetic.

The group of active agents may overlap with other groups of further ingredients described above and below, such as the thickening agents and the emulsifiers.

The at least one active agent of the invention is preferably selected from the group of substances having moisturizing and barrier strengthening properties, such as e.g. hydroviton, an emulsion of NMF, chitosan, alginat, pyrrolidone carbonic acid and salts thereof, lactic acid and salts thereof, glycerol, sorbitol, propylene glycol and urea, substances of the group of proteins and protein hydrolysates, such as e.g. collagen, elastin as well as silk protein, substances of the group of glycosaminoglycans, such as e.g. hyaluronic acid, of the group of carbohydrates, such as e.g. pentavitin that corresponds in its composition to the carbohydrate mixture of the human subcomeus layer, and the group of lipids and lipid precursors such as for example ceramides. Further advantageous active agents in the sense of the present invention may be selected from the group of vitamins, such as e.g. panthenol, niacin, α -tocopherol and its esters, vitamin A as well as vitamin C. Moreover, active agents selected from the group of antioxidants, e.g. galates and polyphenols may be used. Urea, hyaluronic acid and pentavitin are preferred substances.

It is further preferred that substances having skin soothing and regenerative action, such as agents promoting wound healing, are employed as active agents, such as e.g. panthenol, panthenol derivatives (e.g., ethyl panthenol), hyaluronic acid, allantoin, bisabolol, dipotassium glycyrrhizinate and phytosterols. Advantageous active agents in the sense of the present invention are also plants and plant extracts. These are e.g. algae, aloe, arnica, barber's rash, comfrey, birch, nettle, calendula, oak, ivy, witch hazel, henna, hop, camomile, ruscus, peppermint, marigold, rosemary, sage, green tea, tea tree, horsetail, thyme and walnut as well as extracts thereof.

Preferably, the matrix layer further comprises allantoin.

In particular, the matrix layer comprises at least one further active agent, in particular allantoin, in an amount in the range of from 0.01 to 5 % by weight, more preferably in the range of from 0.02 to 4 % by weight, more preferably in the range of from 0.1 to 3 % by weight, more preferably in the range of from 0.3 to 2 % by weight, more preferably in the range of from 0.5 to 1.5 % by weight, and most preferably in the range of from 0.9 to 1.1 % by weight, such as preferably 1.0 % by weight, based on the total weight of the matrix layer.

The matrix layer preferably has a thickness in a range from 20 μm to 100 μm and preferably in a range from 25 μm to 80 μm , more preferably in the range from 30 μm to 60 μm , and more preferably of 40 μm .

Thus, the present invention also relates to a patch, as described above, and a patch obtainable or obtained by the above described method, wherein the matrix layer has a thickness in a range from 20 µm to 100 µm.

- 5 The matrix layer may comprise a rectangular surface if seen in a direction of the layer composition. For example, the surface of the matrix layer may comprise a length of 12 cm and a width of 3 cm. It is to be noted that the term rectangular also encompasses slight deviations from an exact rectangular shape. For example, the surface may comprise rounded edges.

10

The backing liner:

As described above, the patch according to the invention comprises a backing liner.

- Preferably, said backing liner is at least partially made of an occlusive material. The term “occlusive” in the context of the present invention refers to materials that are substantially
15 oxygen and vapor impermeable and liquid impermeable. Suitable occlusive materials preferably have an moisture vapor transmission rate (MVTR) of less than 500, such as in the range of from 0 to 500, more preferably of less than 400, more preferably of less than 300, more preferably of less than 200, measured according to European testing standard EN 13726-2:2002 ‘Test methods for primary wound dressings, part 2: Moisture vapour
20 transmission rate of permeable film dressings’ specified as mass water (in gram), which evaporates during 24 hours through an area of 1 square meter test material.

The weighing difference of the test vessel before and after the measuring time has to be calculated according to the following equation:

25

$$MVTR = \frac{(W1-W2)*Fa*24}{t}$$

W1= mass prior testing [g]

W2 = mass after testing [g]

30

t = Testing time [h]

Fa = factor to convert the test area to 1 m²

- In particular, the backing liner comprises films of metal foil or polymers such as polyvinylidene chloride, polyester, polyethylene terephthalate, polyurethane, polyvinyl fluoride or polyvinyl chloride, polyolefin, polyethylene, polypropylene, PTFE or
35 nitrocellulose. Other suitable polymeric materials include water soluble polymers such as polyvinylpyrrolidones, polyvinyl-alcohols and the like.

Preferably, the polymer is a polyolefine. Suitable polyolefins are, e.g., polyethylenes (with and without acetate moieties, e.g., ethylene vinyl acetate), polypropylenes and the like.

More preferably, the backing liner is a foam liner, preferably a foam liner comprising a polyolefinic foam, more preferably a polyethylene foam.

- 5 Preferably, the backing liner fully covers a surface of the matrix layer facing the backing liner. Thus, the matrix layer is reliably protected and the occlusive effect is enhanced.

Preferably, the backing liner comprises a greater thickness than the matrix layer. This further improves the occlusive characteristics.

- 10 For example, the backing liner comprises a thickness in a range from 150 μm to 500 μm and preferably in a range from 200 μm to 400 μm , more preferably in the range from 200 μm to 400 μm and still more preferably 300 μm .

- 15 The backing liner may comprise a rectangular surface if seen in a direction of the layer composition. For example, the surface of the backing liner may comprise a length of 12 cm and a width of 3 cm. It is to be noted that the term rectangular also encompasses slight deviations from an exact rectangular shape. For example, the surface may comprise rounded edges.

Preferably, the backing liner is adhered to the matrix layer. For example, the backing liner is permanently adhered to the matrix layer. This prevents an unwanted release of the backing liner and an unwanted release of the active agents of the matrix layer.

20 The release liner

- 25 The release liner may comprise a rectangular surface if seen in a direction of the layer composition. For example, the surface of the backing liner may comprise a length of 13 cm and a width of 4 cm. It is to be noted that the term rectangular also encompasses slight deviations from an exact rectangular shape. For example, the surface may comprise rounded edges.

Preferably, the release liner is at least partially siliconized. For example, a top side of the release liner facing and contacting the matrix layer may be siliconized. This facilitates the release of the release liner from the matrix layer for using the patch.

- 30 Preferably, the release liner comprises a greater surface area than a surface of the matrix layer facing the release liner as mentioned above. This reliably protects the matrix layer from contamination.

For example, the release liner protrudes from the matrix layer in at least one direction being perpendicular with respect to a direction of the layer composition. More preferably, the matrix layer comprises side faces and the release liner protrudes from the side faces in a direction being perpendicular with respect to a direction of the layer composition.

- 5 Preferably, the matrix layer is disposed substantially symmetrically on the release liner. For example, the release liner may protrude from all side faces of the matrix layer at 5 mm. This reliably protects the matrix layer from contamination.

The patch has preferably a bond strength of from 0.2 to 5 N/cm, more preferably of from 0.2 to 3 N/cm, preferably 1 N/cm, measured by FTM-2 (90 ° peel test).

- 10 The active substances present in the matrix layer are preferably released with a release rate in the range of from 10 to 100 %, more preferably in the range of from 20 to 100 %, more preferably in the range of from 50 to 100 %, based on the total amount of each active ingredient present in the patch. Thus, the onion extract is preferably released with a release rate in the range of from 5 to 100 %, more preferably in the range of from 10 to 100 %, more preferably in the range of from 20 to 100 %, more preferably in the range of from 30 to 100 %, more preferably in the range of from 40 to 100 %, more preferably in the range of from 50 to 100 %, based on the total amount of the onion extract present in the patch. Further, allantoin is preferably released with a release rate in the range of from 10 to 100 %, more preferably in the range of from 20 to 100 %, more preferably in the range of from 50 to 100 %, based on the total amount of allantoin present in the patch. The active ingredients are thereby preferably released over a time range of from 4 to 8 h, preferably of from 5 to 7 h, preferably over around 6 h.

Method for manufacturing a patch

- As described above, the present invention also relates to a method for manufacturing a patch, and to a patch obtained or obtainable by said method, wherein the method comprises the following steps:

- a) providing the release liner,
b) applying a coating mass comprising an onion extract (A*) and
-- an acrylate based polymer (B), or
30 -- a thermoplastic hot melt adhesive composition (B**) to the release liner,
c) drying the release liner and the coating mass applied thereto such that the matrix layer is formed on the release layer, said matrix layer comprising an onion extract (A) and
35 -- an acrylate based polymer (B), or

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-- a thermoplastic hot melt adhesive (B*)

d) and covering the matrix layer by means of the backing liner.

The coating mass preferably comprises the onion extract (A*) and the acrylate based polymer (B) or the thermoplastic hot melt adhesive composition (B*).

5 The acrylate based polymer is preferably provided in a solution or dispersion comprising at least one solvent S[#]. Thus, the method preferably comprises

a) providing the release liner,

b) applying a coating mass comprising an onion extract (A*) and

-- and a mixture comprising an acrylate based polymer (B) and a solvent S[#], or

10 -- a thermoplastic hot melt adhesive composition (B**)

to the release liner,

c) drying the release liner and the coating mass applied thereto such that the matrix layer is formed on the release layer, said matrix layer comprising an onion extract (A) and

15 -- an acrylate based polymer (B), or

-- a thermoplastic hot melt adhesive (B*).

The solvent S[#] is preferably an organic solvent, preferably an organic solvent selected from the group consisting of DMSO, hexane, toluene, xylene, cyclohexane, methylalcohol, isopropanol, 2,4 pentadione, ethyl acetate, heptane and mixtures of two or more thereof,
20 preferably ethyl acetate and/or heptane.

As described above, the thermoplastic hot melt adhesive composition (B**) is preferably mixed with at least one solvent S^{hm}.

Preferably, the coating mass further comprises the at least one emulsifier. More preferably, the coating mass further comprises allantoin. Further, preferably, the coating mass may
25 comprise at least one additional solvent, such as a solvent selected from the group consisting of ethylacetate, DMSO, heptane, ethanol, water and mixtures of two or more thereof, in addition to S[#] or S^{hm}.

Preferably, before depositing the coating mass on the release liner, the coating mass is homogenized. Suitable methods for homogenizing the mass are known to those skilled in
30 the art.

Preferably, in a first step, the onion extract and part of the polymer (B) or the thermoplastic hot melt adhesive composition (B**) are homogenized to give a mixture M1.

The homogenization in case of (B**) is preferably carried out in the presence of S^{hm}, preferably in ethyl acetate and/or heptane, as described above. The homogenization in case

of (B) is preferably carried out in the presence of at least one solvent, optionally in addition to $S^\#$, preferably in the presence of ethyl acetate and/or heptane.

Likewise, part of the polymer (B) or of the thermoplastic hot melt adhesive composition (B^{**}) and the allantoin are homogenized to give mixture M2. The homogenization in case of (B^{**}) is preferably carried out in the presence of S^{hm} , preferably in ethyl acetate and/or heptane, and additionally in the presence of DMSO. The homogenization in case of (B) is also preferably carried out in the presence of at least one solvent, optionally in addition to $S^\#$, preferably in the presence of DMSO.

Preferably, to both mixtures an emulsifier is added.

Subsequent to the homogenization steps, M1 and M2 are mixed together, and preferably homogenized again to give the coating mass, said coating mass preferably comprising the at least one solvent L which is added in the first step and/or in the second step as described above, wherein the solvent is selected from the group consisting of ethylacetate, DMSO, heptane, ethanol, water and mixtures of two or more thereof, preferably wherein the solvent is a mixture of DMSO and ethanol, and wherein said coating mass optionally comprises $S^\#$ or S^{hm} .

According to an alternative preferred embodiment, allantoin is dissolved in DMSO. Subsequently, the polymer (B), optionally comprising $S^\#$, or the thermoplastic hot melt adhesive composition (B^{**}) is mixed with a solvent, such as an organic solvent, such as an organic solvent selected from the group consisting of preferably an organic solvent selected from the group consisting of DMSO, hexane, toluene, xylene, cyclohexane, methylalcohol, isopropanol, 2,4 pentadione, ethyl acetate, heptane and mixtures of two or more thereof, more preferably ethyl acetate and/or heptane. Then, preferably, the other components are added stepwise and the mixture is homogenized to give the coating mass.

As mentioned above, the thermoplastic hot melt adhesive composition (B^{**}) is preferably not melted in order to apply the mass onto the release liner but dispersed or dissolved in the solvent S^{hm} .

Preferably, the coating mass is evenly applied to the release liner by means of a coating knife. This facilitates the formation of a matrix layer comprising a constant thickness. Thus, the active agents may be evenly released to the patient.

The drying is preferably carried out at a temperature in the range of from 30 to 150 °C, wherein the temperature may be varied or held essentially constant. Preferably, the temperature is continuously or stepwise increased during the drying step. Preferably, the drying is carried out in four drying zones having different temperatures. For examples, the four zones may comprise temperatures in a range from 30 °C to 150 °, preferably in a

range from 40 °C to 140 °C and more preferably in a range from 50 °C to 120 °C. The temperature in each zone may be varied or held essentially constant. Further, the temperature may preferably increase from the first zone to the fourth zone. The drying may preferably be carried out over 15 to 20 minutes. Preferably, in the drying step, substantially all of the solvent present in the coating mass and/or the onion extract is removed. "Substantially all" is denoted to mean preferably at least 98 % by weight, more preferably at least 99 % by weight, more preferably at least 99.9 % by weight, more preferably all of the solvent is removed.

Preferably, the drying is carried out in four temperature zones, wherein in the first zone the temperature is in the range of from 35 °C to 45 °C, in the second zone the temperature is in the range of from 45 °C to 55 °C, in the third zone the temperature is in the range of from 85 °C to 95 °C, and wherein in the fourth zone the temperature is in the range of from 115 °C to 125 °C. Such drying process is e.g. carried out in an oven in which the temperature is increased stepwise to achieve these different temperature zones.

Preferably, the drying in step (c) is carried out in a continuous coating line having four drying zones. Preferably, in this coating line, the drying is carried out with a web speed in the range of from 1.3 m/min to 1.8 m/min.

Preferably, the backing liner, the matrix layer and the release liner form a laminate, wherein the laminate is die cut so as to form the patch. Thus, the form of the patch is constant. Further, the die cutting may be carried out so as to die cut a plurality of patches which improves the production efficiency.

The backing liner and the matrix layer are die cut in a first die cutting step and the release liner is die cut in a second die cutting step, wherein the second die cutting step is carried out such that the release liner comprises a greater surface area than a surface of the matrix layer facing the release liner. Thus, the release liner protrudes from the matrix layer and protects the same in a reliable manner.

For example, the matrix layer comprises side faces and the second die cutting step is carried out such that the release liner protrudes from the side faces in a direction being perpendicular with respect to a direction of the layer composition. Thus, the release liner protrudes from all side faces from the matrix layer.

The release liner is die cut in a third die cutting step so as to form a release means in the release liner. The provision of a release means helps a user of the patch to release the release liner from the matrix layer.

The method may further comprise a sealing step, wherein the patch is sealed in a foil. Accordingly, the patch is reliably protected during storage such that the patch is prevented from being adversely influenced.

The method may further comprise a foil die cutting step, wherein the foil is die cut so as to
5 form a pouch containing the patch. Thus, the patch may be packed in a single step.

Preventing or treating scars

It is to be understood that the preparation of the patch preferably takes place under GMP
10 standardized conditions in order to ensure quality, pharmaceutical security, and effectiveness of the medical device. Further criteria for an ingredient being pharmaceutically acceptable can be derived from approval regulations by a regulatory agency or other generally recognized pharmacopoeias.

The patch according to the present invention is preferably used in treating and/or
15 preventing a scar.

The term “scar” is understood by the skilled person. As used herein, the term, preferably, refers to an abnormal morphological structure which results from a wound, in particular from wounds such as cuts, lacerations, abrasions, gunshot wounds, traumatic skin injury, penetration wounds, acne, operation wounds and burns. A scar typically comprises fibrous
20 tissue. Preferably, the term “scar” includes hypertrophic scars, atrophic scars, and keloid scars. Atrophic scars are flat and depressed below the surrounding skin as a valley or hole. Usually, they are caused when underlying structures which support the skin, e.g. fat tissue or muscle tissue are lost. Hypertrophic scars are elevated scars. Hypertrophic scars occur when the body overproduces collagen. Thereby, the scar is raised above the surrounding
25 skin. Keloid scars are elevated scars that spread beyond the margins of the original wound and invade the surrounding normal skin in a way that is site specific, and often contain whorls of collagen arranged in an abnormal fashion. As laid out elsewhere herein, it is particularly contemplated to treat scars shortly after scar formation. Moreover, it is preferred to treat scars which have been present over a longer period at the time at which
30 treatment is initiated.

Moreover, the term “scar”, preferably, also includes stretch marks. Stretch marks (frequently also referred to as striae) are a form of scarring caused by the overstretching of skin. This stretching disrupts the normal production of collagen and a scar results. Preferably, stretch marks are caused by rapid growth or rapid weight gain, in particular as a

consequence of pregnancy. The term “stretch marks” preferably, includes striae distensae, striae atrophicans, striae rubra (red stretch marks) and striae alba (white stretch marks).

The terms “treating a scar” or “treatment of a scars”, preferably, refers to the therapeutic treatment or the cosmetic treatment of a scar. The cosmetic treatment, preferably,
5 comprises the administration of the composition of the present invention to a subject with a scar for improving the appearance of scar tissue and/or for reduction of scar tissue. The improvement of appearance of scar tissue, preferably, refers to reduced discoloration, decreased hyperpigmentation, softening of scar tissue, decreased erythma, or improved aesthetic appearance of the scar. The reduction of scar tissue, preferably, refers to reduced
10 scar height and/or scar size.

Preferably, the terms “treating a scar” or “treatment of scars” comprise softening of scar tissue thus improving softness of scar tissue, improved aesthetic appearance of the scar, and, more preferably, reduced discoloration of the scar. Preferably, the discoloration of a scar is reduced if the redness of the scar is reduced. By reducing the discoloration, the scar
15 becomes less visible.

As set forth above, the terms “treating a scar” or “treatment of scars” also refer to the therapeutic treatment of a scar, in particular include amelioration or prevention of pain (in particular scar pain) and amelioration or prevention of pruritus.

The term “subject” as used herein relates to animals, preferably mammals, and, more
20 preferably, humans.

Preferably, the patch of the present invention is applied onto the scar, i.e. to the scar tissue, or to the stretch mark.

According to a further embodiment of the invention, the patch of the present invention is applied onto the wound during the wound healing process. According to another
25 embodiment of the invention, the patch of the present invention is applied onto the skin after completion of the wound healing process. In particular, the patch of the present invention can be applied onto the skin shortly after scar formation, e.g. within one month after scar formation. Further, it is contemplated to treat older scars which have been present over a longer period at the time at which treatment is initiated. Thus, the scar,
30 preferably, has been present for at least one month, more preferably, for at least six months, or, most preferably, for at least one year at the time at which treatment is initiated.

Preferably, the composition of the present invention is applied over night, i.e. for at least 6, preferably at least 8 h.

It is to be understood that the composition of the present invention is applied for a time effective to allow for the treatment or prevention of a scar.

5 The patch of the present invention can be also used for preventing scars, i.e. for preventing scar formation. The term “preventing” as used herein, preferably, refers to applying the patch to a subject in order to prevent or, in particular, to reduce *de novo* formation of scars. Moreover, the prevention of scars preferably also comprises the amelioration or prevention of pain and/or pruritus during scar formation. In order to prevent scars, the patch is administered to a wound while the wound is still in the process of healing and, thus, during completion of the wound healing process.

10 According to further embodiments of the invention, the patch of the present invention further exhibits a bactericidal activity. The term “bactericidal activity” as used herein, preferably refers to an activity which is capable killing bacterial cells. The patch of the present invention may, if administered to a subject, advantageously allow for treating and preventing scars and for killing bacterial cells in the scar tissue.

15 Also, the patch of the present invention may further prevent excessive fibroblast proliferation.

Moreover, the patch of the present invention, preferably, further exhibits anti-inflammatory activity.

20 The present invention also relates to a method for treating and/or preventing a scar in a subject in need thereof comprising applying to the skin of said subject the patch of the present invention.

The present invention also relates to the use of the patch of the present invention for treating and/or preventing a scar in a subject in need thereof.

25 The present invention also relates to a method for the cosmetic treatment of a scar in a subject in need thereof comprising applying to the skin of said subject the patch of the present invention.

The present invention also relates to the use of the patch of the present invention for the cosmetic treatment of a scar in a subject in need thereof.

30 As set forth above, cosmetic treatment, preferably, comprises the administration of the patch of the present invention to a subject with a scar for improving the appearance of scar tissue and/or for reduction of scar tissue. In particular, the term comprises softening of scar tissue, thus improving softness of scar tissue, improved aesthetic appearance of the scar, and reduced discoloration of the scar.

In the following, especially preferred embodiments of the present invention are described:

1. Patch comprising a layer composition, wherein the layer composition comprises at least
 - a backing liner,
 - a matrix layer comprising an onion extract (A), and
 - 5 - an acrylate based polymer (B), or
 - a thermoplastic hot melt adhesive (B*),
 - and a release liner, whereinthe matrix layer is disposed between the backing liner and the release liner such that the matrix layer is contacted by the backing liner and the release liner on opposite sides thereof, wherein the release liner is releasable from the matrix layer.
- 10 2. Patch according to embodiment 1, wherein the matrix layer comprises the onion extract (A) in an amount in the range of from 0.01 to 5 % by weight, based on the total weight of the matrix layer and calculated as the dry onion extract.
- 15 3. Patch according to embodiment 1 or 2, wherein the onion extract (A) is an *Allium cepa* extract.
- 20 4. Patch according to any one of embodiments 1 to 3, wherein the matrix layer comprises an acrylate based polymer (B) and an onion extract (A), and wherein the polymer (B) is a acrylate-vinylacetate based polymer comprising building blocks derived from the monomeric components acrylate (B1) and vinylacetate (B2).
- 25 5. Patch according to any one of embodiments 1 to 3, wherein the matrix layer comprises a thermoplastic hot melt adhesive (B*), and an onion extract (A), and wherein the polymer (B*) is a hot melt thermoplastic rubber, preferably comprising a styrene polymer, a tackifying resin and a plasticizer.
- 30 6. Patch according to any one of embodiments 1 to 3 and 5, wherein the matrix layer comprises a thermoplastic hot melt adhesive (B*), and an onion extract (A), wherein the matrix layer is obtained, by
 - dissolving or dispersing a thermoplastic hot melt adhesive composition (B**) in a
 - 35 solvent S^{hm} ,
 - mixing this solution or dispersion with at least an onion extract (A*) to give a coating mass,
 - applying the coating mass onto a release liner, and

- drying the release liner and the coating mass applied thereto such that the matrix layer comprising an onion extract (A) and the thermoplastic hot melt adhesive (B*) is formed on the release layer, and comprising an onion extract (A*) and an thermoplastic hot melt adhesive (B*) to the release liner.

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7. Patch according to embodiment 6, wherein the thermoplastic hot melt adhesive composition B** is not melted prior to the application of the coating mass onto the release liner.

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8. Patch according to any one of embodiments 1 to 7, wherein the matrix layer further comprises at least one emulsifier, preferably caprylocaproyl macrogol glyceride.

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9. Patch according to embodiment 8, wherein the matrix layer comprises the at least one emulsifier in an amount in the range of from 0.01 to 5 % by weight, based on the total weight of the matrix layer.

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10. Patch according to any one of embodiments 1 to 9, wherein the matrix layer further comprises allantoin, preferably in an amount in the range of from 0.01 to 5 % by weight, based on the total weight of the matrix layer.

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11. Patch according to any one of embodiments 1 to 10, wherein the release liner comprises a greater surface area than a surface of the matrix layer facing the release liner.

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12. Patch according to any one of embodiments 1 to 11, wherein the release liner protrudes from the matrix layer in at least one direction being perpendicular with respect to a direction of the layer composition.

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13. Patch according to any one of embodiments 1 to 12, wherein the matrix layer comprises side faces and the release liner protrudes from the side faces in a direction being perpendicular with respect to a direction of the layer composition.

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14. Patch according to any one of embodiments 1 to 13, wherein the matrix layer is disposed substantially symmetrically on the release liner.

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15. Patch according to any one of embodiments 1 to 14, wherein the backing liner fully covers a surface of the matrix facing the baking liner.

16. Patch according to any to any one of embodiments 1 to 15, wherein the backing liner is at least partially made of an occlusive material.
17. Patch according to any one of embodiments 1 to 16, wherein the backing liner is a foam liner, preferably a foam liner comprising a polyolefin.
18. Patch according to any one of embodiments 1 to 17, wherein the backing liner comprises a greater thickness than the matrix layer.
19. Patch according to any one of embodiments 1 to 18, wherein the backing liner comprises a thickness in a range of from 150 μm to 500 μm and preferably in a range of from 200 μm to 400 μm , more preferably in the range of from 200 μm to 400 μm and still more preferably 300 μm .
20. Patch according to any one of embodiments 1 to 19, wherein the release liner is at least partially siliconized.
21. Patch according to any one of embodiments 1 to 20, wherein the release liner comprises a thickness in a range of from 25 μm to 75 μm .
22. Patch according to any one of embodiments 1 to 21, wherein the backing liner and/or the matrix layer and/or the release liner comprises a rectangular surface if seen in a direction of the layer composition.
23. Patch according to any one of embodiments 1 to 22, wherein the backing liner is adhered to the matrix layer.
24. Patch according to any one of embodiments 1 to 23, wherein the backing liner is permanently adhered to the matrix layer.
25. Method for manufacturing a patch comprising the following steps:
- (a) providing the release liner,
 - (b) applying a coating mass comprising an onion extract (A*) and
 - an acrylate based polymer (B), or
 - a thermoplastic hot melt adhesive composition (B**)to the release liner,
 - (c) drying the release liner and the coating mass applied thereto such that the matrix layer is formed on the release layer, said matrix layer comprising an onion extract (A) and

- an acrylate based polymer (B), or
 - a thermoplastic hot melt adhesive (B*)
- (d) and covering the matrix layer by means of the backing liner.

5 26. Method according to embodiment 25, wherein the onion extract (A*) of step (b) is obtainable by a process comprising the steps

(a1) extracting fresh or dried onions, preferably *Allium cepa*, with a solvent S₁ comprising at least one alcohol to give a liquid phase L₁ and a solid residue R₀,

10 (b1) separating the liquid phase L₁ from the solid residue R₀,

(c1) evaporating the liquid phase L₁ to give a residue R₁,

(d1) redissolving the residue R₁ in a solvent S₂ comprising at least one alcohol and water to give the onion extract (A*)

15 27. Method according to embodiment 26, wherein the coating mass comprises a thermoplastic hot melt adhesive, and wherein the step (a) comprises

- dissolving or dispersing the thermoplastic hot melt adhesive composition (B**) in a solvent S^{hm}, mixing this solution or dispersion with at least an onion extract (A*)

to give the coating mass, and applying said coating mass to the release liner.

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28. Method according to any one of embodiments 22 to 27, wherein the coating mass of step (b) further comprises at least one emulsifier.

25 29. Method according to any one of embodiments 25 to 28, wherein the coating mass of step (b) further comprises allantoin.

30. Method according to any one of embodiments 25 to 29, wherein in step (b) the coating mass is evenly applied to the release liner by means of a coating knife.

30 31. Method according to any one of embodiments 25 to 30, wherein the drying in step (c) is carried out in four temperature zones having different temperatures.

35 32. The method according to embodiment 31, wherein in the first zone the temperature is in the range of from 35 °C to 45 °C, in the second zone the temperature is in the range of from 45 °C to 55 °C, in the third zone the temperature is in the range of from 85 °C to 95 °C, and wherein in the fourth zone the temperature is in the range of from 115 °C to 125 °C.

33. The method according to embodiment 31 or 32, wherein the drying in step (c) is carried out in a continuous coating line having four drying zones and the drying is performed with a web speed in the range of from 1.3 m/min to 1.8 m/min.

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34. Method according to any one of embodiments 25 to 33, wherein the backing liner, the matrix layer and the release liner form a laminate, wherein the laminate is die cut so as to form the patch.

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35. Method according to embodiment 34, wherein the backing liner and the matrix layer are die cut in a first die cutting step and the release liner is die cut in a second die cutting step, wherein the second die cutting step is carried out such that the release liner comprises a greater surface area than a surface of the matrix layer facing the release liner.

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36. Method according to embodiment 34 or 35, wherein the matrix layer comprises side faces and the second die cutting step is carried out such that the release liner protrudes from the side faces in a direction being perpendicular with respect to a direction of the layer composition.

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37. Method according to any one of embodiments 35 to 36, wherein the release liner is die cut in a third die cutting step so as to form a release means in the release liner.

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38. Method according to any one of embodiments 25 to 37, further comprising a sealing step, wherein the patch is sealed in a foil.

39. Method according to any one of embodiments 25 to 38, further comprising a foil die cutting step, wherein the foil is die cut so as to form a pouch containing the patch.

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40. Patch obtained or obtainable by a method according to any one of embodiments 25 to 39.

41. Patch according to any one of embodiments 1 to 24 or embodiment 40 for use in treating and/or preventing a scar.

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Figures:

Further details and aspects of the present invention may be realized from the below description of preferred embodiments which are schematically shown in the drawings, in which:

- 5 Fig. 1 shows a cross-sectional view of a patch according to an embodiment of the present invention;

Fig. 2 shows a top view of the patch;

Fig. 3 shows a first manufacturing step for manufacturing a patch according to an embodiment of the present invention;

- 10 Fig. 4 shows a second manufacturing step for manufacturing a patch according to an embodiment of the present invention;

Fig. 5 shows a third manufacturing step for manufacturing a patch according to an embodiment of the present invention;

- 15 Fig. 6 shows a fourth manufacturing step for manufacturing a patch according to an embodiment of the present invention;

Fig. 7 shows a fifth manufacturing step for manufacturing a patch according to an embodiment of the present invention;

Fig. 8 shows a sixth manufacturing step for manufacturing a patch according to an embodiment of the present invention; and

- 20 Fig. 9 shows a seventh manufacturing step for manufacturing a patch according to an embodiment of the present invention.

Examples: Detailed description of the patch

- 25 Fig. 1 shows a schematic cross-section of a patch 10 according to an embodiment of the present invention. The patch 10 may be used for the treatment of scars. The patch 10 comprises a layer composition 12. The layer composition 12 comprises a backing liner 14, a matrix layer 16 and a release liner 18.

The backing liner 14 may be specified as described in example 1

The matrix layer 16 may be specified as described in example 1

- 30 The release liner 18 may be specified as described in example 1

As shown in Fig. 1, the matrix layer 16 is disposed between the backing liner 14 and the release liner 18 such that the matrix layer 16 is contacted by the backing liner 14 and the release liner 18 on opposite sides thereof. Thus, the matrix layer 16 is sandwiched between the backing liner 14 and the release liner 18. The release liner 18 is releasable from the matrix layer 16. Each of the backing liner 14, the matrix layer 16 and the release liner 18 is formed as a thin cuboid. Thus, the contacting surfaces of the backing liner 14, the matrix layer 16 and the release liner 18 are rectangular. The edges of the rectangular shape may be rounded. Particularly, the matrix layer 16 comprises a top side 20 contacting the backing liner 14, a bottom side 22 contacting the release liner 18 and side faces 24 being perpendicular to the top side 20 and the bottom side 22.

The backing liner 14 fully covers a surface of the matrix layer 16 facing the backing liner 14. In this embodiment, the surface of the matrix layer 16 facing the backing liner 14 is the top side 20 as mentioned above. The backing liner 14 may comprise a length of 12 cm and a width of 3 cm. Thus, the contacting surface area is 36 cm^2 . Further, the backing liner 14 may comprise a thickness in a range from 150 μm to 500 μm and preferably in a range from 200 μm to 400 μm , more preferably in the range from 200 μm to 400 μm . For example, the backing liner comprises a thickness of 300 μm . The backing liner 14 comprises a greater thickness than the matrix layer 16 as will be described in more detail below. The backing liner 14 is at least partially made of an occlusive material. The backing liner 14 is adhered to the matrix layer 16. Preferably, the backing liner 14 is permanently adhered to the matrix layer 16.

The release liner 18 comprises a greater surface area than a surface of the matrix layer 16 facing the release liner 18. In this embodiment, the surface of the matrix layer 16 facing the release liner 18 is the bottom side as mentioned above. Fig. 2 shows a top view of the patch 10. As shown in Fig. 2, the release liner 18 protrudes from the matrix layer 16 in at least one direction being perpendicular with respect to a direction of the layer composition 12. Particularly, the release liner 18 protrudes from the side faces 24 of the matrix layer 16 in a direction being perpendicular with respect to a direction of the layer composition 12. Thus, the matrix layer 16 is disposed substantially symmetrically on the release liner 18. With other words, the matrix layer 16 is evenly spaced apart from edges 26 of the release liner 18. For example, the release liner 18 comprises a length of 14 cm and a width of 4 cm. Thus, the release liner 18 evenly protrudes from the side faces 24 of the matrix layer 16 at 5 mm. The release liner 18 comprises a thickness in a range from 25 μm to 75 μm . For example, the release liner 18 comprises a thickness of 50 μm . The release liner 18 is at least partially siliconized. For example, a top side 28 of the release liner 18, onto which the matrix layer 16 is disposed, is siliconized. This ensures that the release liner 18 may be easily released from the matrix layer 16 for using the patch 10. The release liner 18 may

further comprise a release means die cut therein which facilitates releasing of the release liner 18. For example, the release liner 18 may comprise a latch or a perforation.

The patch 10 may be manufactured as will be explained in more detail below. As shown in Fig. 3, which shows a first step of the manufacturing process, a coating mass 30 may be provided. For example, the coating mass may be provided by stirring the above ingredients in a container 32 such as a vessel.

Fig. 4 shows a second step of the manufacturing process. A release liner 18 as explained above is provided. The coating mass 30 is applied to the release liner 18. More particularly, the coating mass 30 is applied to the siliconized top side 28 of the release liner 18. Further, the coating mass 30 is evenly applied to the release liner 18 by means of a coating knife 34. Alternatively, a nozzle may be used for applying the coating mass 30. The coating mass 30 is applied to the release liner 18 so as to have a thickness in a range from 20 μm to 100 μm and preferably in a range from 25 μm to 80 μm , more preferably in the range from 30 μm to 60 μm , and more preferably of 40 μm .

As shown in Fig. 5, which shows a third step of the manufacturing process, the coating mass 30 may be applied to the release liner 18 such that the release liner 18 protrudes from edges 36 of the coating mass 30. With other words, the release liner 18 comprises a greater surface area than a surface area of the coating mass 30 contacting the release liner 18. Further, the release liner 18 and the coating mass 30 applied thereto are dried such that solvent is released from the coating mass 30 and the above described matrix layer 16 is formed on the release liner 18. The drying may be carried out in a drying tunnel having four drying zones. The temperature in the four drying zones may be in a preferred range of from 50 °C to 120 °C over 15 to 20 minutes. The temperature may increase from the first zone to the fourth zone which corresponds to an increase in the conveying direction of the release liner 18 and the coating mass 30. The backing liner 14 and/or the matrix layer 16 may be provided with an adhesive such that the backing liner 14 is permanently adhered to the matrix layer 16.

Fig. 6 shows a fourth step of the manufacturing process. As shown in Fig. 6, the above described backing liner 14 is applied to the matrix layer 16 so as to cover the same. More particularly, the backing liner 14 may be applied to the matrix layer 16 by means of a lamination roll 38 which facilitates an even pressure distribution onto the backing liner 14 and the matrix layer 16. Thus, the backing liner 14, the matrix layer 16 and the release liner 18 form a laminate 40 which may be considered as a large patch band. Subsequently, the laminate 40 may be reeled up and transported to a die cutting station. Needless to say, the laminate 40 may be die cut immediately following the fourth step.

Fig. 7 shows a fifth step of the manufacturing process. As shown in Fig. 7, the laminate 40 is die cut by means of a die cutting tool 42. More particularly, the backing liner 14 and the matrix layer 16 are die cut in a first die cutting step such that the backing liner 14 and the matrix layer 16 comprise the above surface area. Then, the release liner 18 is die cut in a second die cutting step such that the release liner comprises the above surface area being greater than the surface area of the backing liner 14 and the matrix layer 16 facing the release liner 18. With other words, the release liner 18 evenly protrudes from the side faces 24 of the matrix layer 16 as explained above. It is explicitly mentioned that the second die cutting step may be made before the first die cutting step. Thus, from the laminate, a plurality of patches 10 is die cut having the above described layer composition 12. Further, the release liner 18 of each patch 10 protrudes from the side faces 24 of the matrix layer in a direction perpendicular with respect to a direction of the layer composition 12. Furthermore, the release liner 18 may be die cut in a third die cutting step so as to form a release means as described above.

Fig. 8 shows a sixth step of the manufacturing process. As shown in Fig. 8, the process may further comprise a sealing step. In the sealing step, the patch 10 is sealed in a foil 44. Thus, the foil completely houses the patch 10 in a hermetical manner.

Fig. 9 shows a seventh step of the manufacturing process. As shown in Fig. 9, the process may further comprise a foil die cutting step. In the foil die cutting step, the foil 44 containing the patch 10 is die cut so as to form a pouch 46 containing the patch 10. Thus, The patch 10 is packed and the pouch 46 may be opened for taking out the patch 10 for use.

The laminate 40 may be cut before the die cutting steps to provide a plurality of laminates. The width of the cut laminate 40 may be adapted to the width of the width of the patch to be die cut.

Example 1: Preparation of an acrylate based patch comprising onion extract:

0.4 g allantoin were predissolved in DMSO (10 %) and were added to 43.96 g Duro Tak 87-2194 (solid content 43 %). A second preparation contained 1.96 g onion extract (30 % by weight in aqueous ethanolic solution (10-16 Vol-% ethanol in water), 1.2 g Labrasol and 43.96 g Duro Tak 87-2194. Both mixtures were merged together and adjusted with ethyl acetate to a solid content of 42.6 %. The mixture was stirred until homogenous by means of a mechanical stirrer. This coating mass was deposited in form of a thin layer by means of a suitable coating device (e.g. doctor blade) on an inert protective foil (PET film 50 µm, siliconized) and dried for 15-20 min at 50-120 °C. Subsequent to the drying step,

the adhesive layer (area weight of 50 g/m²) of the double layered laminate was laminated with a second foil (backing layer, e.g. polyolefine).

From the three layered laminate, patches of respective size (in this case 36 cm²) were die cut by means of a rotating punch.

- 5 The onion extract is obtainable for example from Finzelberg Extrakte and described in US 5,885,581.

A patch comprising the following composition was obtained:

		Weight % based on the total weight of the respective layer	Per m ² of the patch [g]
Matrix layer: Thickness (40 µm)	Onion extract	1	0,4
	Polyacrylate-vinylacetate (Duro-Tak 87-2194)	95	38
	Labrasol	3	1,2
	Allantoin	1	0,4
Backing layer Thickness (500 µm)	Foam: Polyethylene foam: Alveolit TEE Z 0800.52		65
Release layer Thickness (50 µm)	PET film 50 µm, siliconized		72

- 10 The patch had an adhesive force of around 0.8 N/cm, measured by FMT-2 with a release rate of allantoin of 19 % and a release of onion extract of 28 %, based on the total weight of each compound in the patch, respectively, and measured after 6 h using HPLC.

Further, the patch was comfortable to wear and easy to remove from the skin while remaining secure in position. Further, biocompatibility according to ISO 10993-5 2009 is given.

Comparative Example 2: Preparation of a silicone based patch comprising onion extract:

		Weight % based on the total weight of the respective layer	Per m ² of the patch [g]
Matrix layer: Thickness (40 µm)	Onion extract	1	0,4
	Silicon soft skin adhesive MG7-9900 Part A + Part B	Part A 49 Part B 49	39,2
	Allantoin	1	0,4
Backing layer Thickness (500 µm)	Foam: Polyethylene foam: Alveolit TEE Z 0800.52		65
Release layer Thickness: (50 µm)	PET film 50 µm, siliconized		72

With silicone patches, no release of the onion extract was observed.

Example 3: Preparation of a hot melt adhesive based patch comprising onion extract:

- 5 Dermatak H542B (Henkel) has been dissolved in an ethylacetat/heptane mixture 1:1 (weight ratio of Dermatak to solvent mixture 1:1).

0.4 g Allantoin were predissolved in DMSO (10 %) and were added to 38,4 g Dermatak (solid content 50 %) ethyl acetate/heptane mixture. A second preparation contained 1.96 g onion extract (30 % by weight in aqueous ethanolic solution (10-16 Vol-% ethanol in water)), 0.8 g Labrasol and 38,4 g Dermatak ethyl acetate/heptane mixture (solid content 50 %). Both mixtures were merged together and adjusted with ethyl acetate to a solid content of 48 %. The mixture was stirred until homogenous by means of a mechanical stirrer. This coating mass was deposited in form of a thin layer by means of a suitable coating device (e.g. doctor blade) on an inert protective foil (PET film 50 µm, siliconized) and dried for 15-20 min at 50-120 °C. Subsequent to the drying step, the adhesive layer (area weight of 50 g/m²) of the double layered laminate was laminated with a second foil (backing layer, e.g. polyolefine).

From the three layered laminate, patches of respective size (in this case 36 cm²) were die cut by means of a rotating punch.

- 20 A patch comprising the following composition was obtained:

		Weight % based on the total weight of the respective layer	Per m ² of the patch [g]
Matrix layer:	Onion extract	1	0,4
Thickness (40 µm)	Dermatak	96	38,4
	Labrasol	2	0,8
	Allantoin	1	0,4
Backing layer	Foam: Polyethylene foam:		65
Thickness (500 µm)	Alveolit TEE Z 0800.52		
Release layer	PET film 50 µm, siliconized		72
Thickness (50 µm)			

Example 4: Influence of drying temperature on onion extract content (cepalin content) :

- 5 Dermatak H542B (Henkel) has been dissolved in an ethylacetat/heptane mixture 1:1 (weight ratio of Dermatak to solvent mixture 1:1).

0.44 Allantoin were predissolved in DMSO (10 %). The Allantoin mixture and 1.96 g onion extract (30 % by weight in aqueous ethanolic solution (10-16 Vol-% ethanol in water)), were added to 70.76 Dermatak ethyl acetate/heptane mixture (solid content 50 %).

- 10 The mixture was adjusted with ethyl acetate to a solid content of 49 % stirred until homogenous by means of a mechanical stirrer. This coating mass was deposited in form of a thin layer by means of a suitable coating device (e.g. doctor blade) on an inert protective foil (PET film 50 µm, siliconized) and dried in dried for 15-20 min at 50-120 °C. Subsequent to the drying step, the adhesive layer (area weight of 50 g/m²) of the double
15 layered laminate was laminated with a second foil (backing layer, e.g. polyolefine).

From the three layered laminate, patches of respective size (in this case 36 cm²) were die cut by means of a rotating punch.

- In all obtained patches, the DMSO content and the cepalin content (content of the onion extract was measured). An optimum combination of a relative high amount of cepalin with a relative low amount of DMSO was obtained when using the temperatures and web speed shown in entry 4 and 5. At very high temperatures, the amount of onion extract was lower (entries 1 to 3), and at lower temperatures, the DMSO content higher (entry 6). Thus, a medium temperature together with a medium or low web speed is particularly advantageous.

Entry	Temperature (°C) zone 1 – zone 2 – zone 3 – zone 4	Web speed [m/min]	DMSO content (weight %, based on the total weight of the matrix layer)	Cepalin content (weight %, based on the total weight of the matrix layer)
1	50 – 90 – 120 – 140	1.3	0	0.6
2	50 – 90 – 120 – 140	1.8	0	0.6
3	50 – 90 – 120 – 140	2.1	0	0.6
4	40 – 50 – 90 – 120	1,3	0.8	1.1
5	40 – 50 – 90 – 120	1,8	1.7	1.2
3	40 – 50 – 65 - 80	1,3	9.3	1.4

Example 5: Further prepared patches

All samples had a release liner consisting of PET 50 micrometer siliconised (Primeliner, Loparex). The samples vary in the adhesive system and the backing layer material, but have all an Allantoin and Onion extract content of 1 %. All versions are summarized in the following table. Each single patch was packed in a peel-able pouch made of a PET-Alu-PP 3-composite layered foil.

The samples were manufactured with the parameter setting described above in example 1 and 3, respectively

Batch	Sample	Adhesiv	Exipients	Backing
C0047	1	DT 87-2677	--	TEE Z 0800.52 Foam
C0048	2	DT 87-2194	3 % Labrasol	TEE Z 0800.52 Foam
C0057	3	Dermatak H524B	--	TEE Z 0800.52 Foam
C0050	4	Dermatak H524B	2 % Solutol	TEE Z 0800.52 Foam
C0051	5	Dermatak H524B	2 % Labrasol	TEE Z 0800.52 Foam
C0058	6	Dermatak H524B	4 % Peceol	Cotran 9720
C0053	7	DT 87-2677	--	Cotran 9720
C0054	8	DT 87-2194	3 % Labrasol	Cotran 9720
C0055	9	Dermatak H524B	--	Cotran 9720
C0056	10	Dermatak H524B	2 % Solutol	Cotran 9720

*C0048 corresponds to example 1, C0051 corresponds to example 3.

Example 6: Cepalin and Allantoin release of the patches according to example 5

The cepalin and allantoin release of the patches prepared according to example 6 was analyzed. The release study was carried out in 120 mL phosphate buffer pH 3 comprising 5% DMSO. The patch was incubated (thereby agitated) for 6h in the phosphate buffer.

Thereafter, the amount of allantoin and cepalin present in the phosphate buffer was measured using HPLC .

Further, the adhesion force of the patches and DMSO content of the matrix layer was determined. The adhesion force was measured using the 90° peel adhesion test (FINAT test method no. 2 (FTM 2)) and the DMSO content using HPLC.

The results are given in the following table:

- 43 -

Batch	Sample	Content Allantoin (%)		Release (%)		Adhesion force (N/cm)	DMSO content (%)
		Allantoin	Cepalin	Allantoin	Cepalin		
C0047	1	0.91	0.49	14.5	94.0	-	-
C0048	2	0.93	1.22	18.9	27.6	0.77	0.09
C0057	3	0.90	0.85	3.8	10.8	-	-
C0050	4	1.02	0.85	50.6	24.7	2.21	0.37
C0051	5	0.83	0.85	4.2	15.2	-	-
C0058	6	1.17	1.10	20.4	24.0	2.03	0.74
C0053	7	1.07	0.49	17.2	86.4	-	-
C0054	8	1.04	1.22	32.6	14.8	0.73	0.09
C0055	9	0.98	0.85	15.4	17.1	2.86	0.39
C0056	10	0.96	0.98	28.5	26.2	2.95	0.28

All patches comprised onion extract and allantoin and were able to release up to 94 % of the total amount of the onion extract as well as of cepalin.

- 5 In particular, samples 2, 4, 6, 8, 9 and 10 showed an advantageous combination of a high amount of allantoin and cepalin within the patches, with a relatively low amount of DMSO and with a relatively high release of cepalin and allantoin when used.

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Claims:

1. Patch comprising a layer composition, wherein the layer composition comprises at least
 - a backing liner,
 - 5 - a matrix layer comprising an onion extract (A), and
 - an acrylate based polymer (B), or
 - a thermoplastic hot melt adhesive (B*),
 - and a release liner, whereinthe matrix layer is disposed between the backing liner and the release liner such that
10 the matrix layer is contacted by the backing liner and the release liner on opposite sides thereof, wherein the release liner is releasable from the matrix layer.
2. Patch according to claim 1, wherein the matrix layer comprises the onion extract (A) in an amount in the range of from 0.01 to 5 % by weight, based on the total weight of the
15 matrix layer and calculated as the dry onion extract.
3. Patch according to claims 1 or 2, wherein the onion extract (A) is an *Allium cepa* extract.
- 20 4. Patch according to any one of claims 1 to 3, wherein the matrix layer comprises an acrylate based polymer (B) and an onion extract (A), and wherein the polymer (B) is a acrylate-vinylacetate based polymer comprising building blocks derived from the monomeric components acrylate (B1) and vinylacetate (B2).
- 25 5. Patch according to any one of claims 1 to 3, wherein the matrix layer comprises a thermoplastic hot melt adhesive (B*), and an onion extract (A), and wherein the polymer (B*) is a hot melt thermoplastic rubber, preferably comprising a styrene polymer, a tackifying resin and a plasticizer.
- 30 6. Patch according to any one of claims 1 to 3 and 5, wherein the matrix layer comprises a thermoplastic hot melt adhesive (B*), and an onion extract (A), wherein the matrix layer is obtained, by
 - dissolving or dispersing a thermoplastic hot melt adhesive composition (B**) in a
35 solvent S^{hm} ,
 - mixing this solution or dispersion with at least an onion extract (A*) to give a coating mass,
 - applying the coating mass onto a release liner, and

- 45 -

- drying the release liner and the coating mass applied thereto such that the matrix layer comprising an onion extract (A) and the thermoplastic hot melt adhesive (B*) is formed on the release layer, and comprising an onion extract (A*) and an thermoplastic hot melt adhesive (B*) to the release liner.

5

7. Patch according to claim 6, wherein the thermoplastic hot melt adhesive composition B** is not melted prior to the application of the coating mass onto the release liner.

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8. Patch according to any one of claims 1 to 7, wherein the matrix layer further comprises allantoin, preferably in an amount in the range of from 0.01 to 5 % by weight, based on the total weight of the matrix layer.

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9. Patch according to any to any one of claims 1 to 8, wherein the backing liner is at least partially made of an occlusive material.

10. Patch according to any one of claims 1 to 9, wherein the backing liner is a foam liner, preferably a foam liner comprising a polyolefin.

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11. Method for manufacturing a patch comprising the following steps:

(a) providing the release liner,

(b) applying a coating mass comprising an onion extract (A*) and

-- an acrylate based polymer (B), or

25

-- a thermoplastic hot melt adhesive composition (B**)

to the release liner,

(c) drying the release liner and the coating mass applied thereto such that the matrix layer is formed on the release layer, said matrix layer comprising an onion extract (A) and

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-- an acrylate based polymer (B), or

-- a thermoplastic hot melt adhesive (B*)

(d) and covering the matrix layer by means of the backing liner.

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12. Method according to claim 11, wherein the onion extract (A*) of step (b) is obtainable by a process comprising the steps

(a1) extracting fresh or dried onions, preferably *Allium cepa*, with a solvent S₁ comprising at least one alcohol to give a liquid phase L₁ and a solid residue R₀,

(b1) separating the liquid phase L₁ from the solid residue R₀,

- (c1) evaporating the liquid phase L_1 to give a residue R_1 ,
- (d1) redissolving the residue R_1 in a solvent S_2 comprising at least one alcohol and water to give the onion extract (A^*)

5 13. Method according to claim 11 or 12, wherein the coating mass comprises a thermoplastic hot melt adhesive, and wherein the step (a) comprises

- dissolving or dispersing the thermoplastic hot melt adhesive composition (B^{**}) in a solvent S^{hm} , mixing this solution or dispersion with at least an onion extract (A^*) to
10 give the coating mass, and applying said coating mass to the release liner.

14. Method according to any one of claims 11 to 13, wherein the drying in step (c) is carried out in four drying zones having different temperatures.

15 15. The method according to claim 14, wherein in the first zone the temperature is in the range of from 35 °C to 45 °C, in the second zone the temperature is in the range of from 45 °C to 55 °C, in the third zone the temperature is in the range of from 85 °C to 95 °C, and wherein in the fourth zone the temperature is in the range of from 115 °C to 125 °C.

20 16. The method according to claim 14 or 15, wherein the drying in step (c) is carried out in a continuous coating line having four temperature zones and the drying is performed with a web speed in the range of from 1.3 m/min to 1.8 m/min.

25 17. Patch obtained or obtainable by a method according to any one of claims 11 to 16.

18. Patch according to any one of claims 1 to 10 or claim 17 for use in treating and/or preventing a scar.

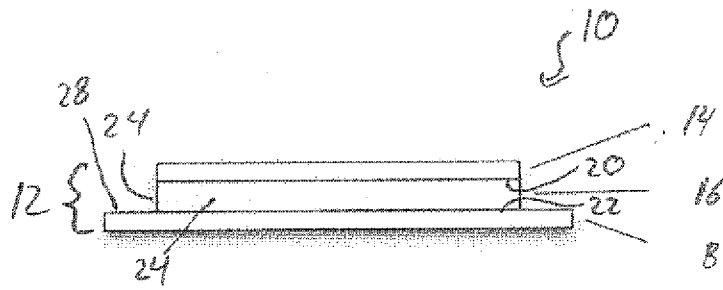


Fig. 1

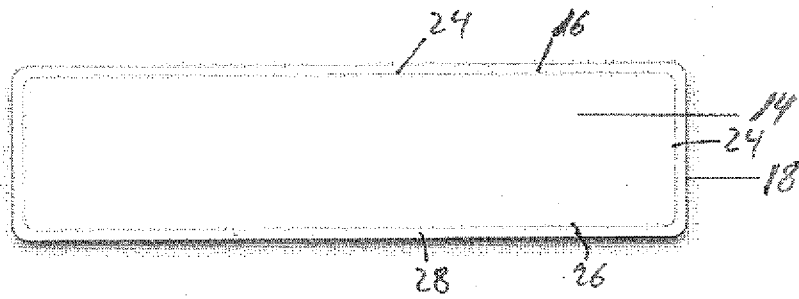


Fig. 2

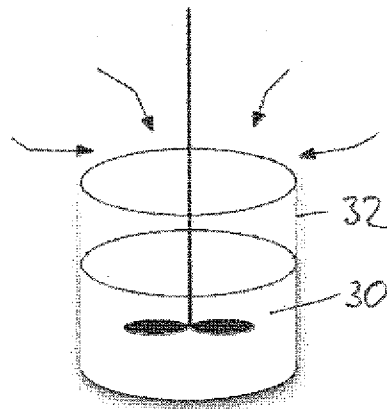


Fig. 3

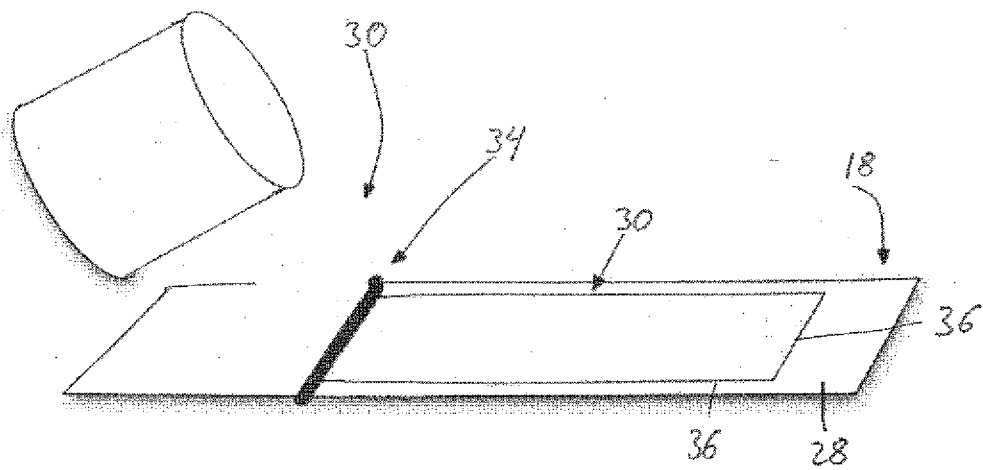


Fig. 4

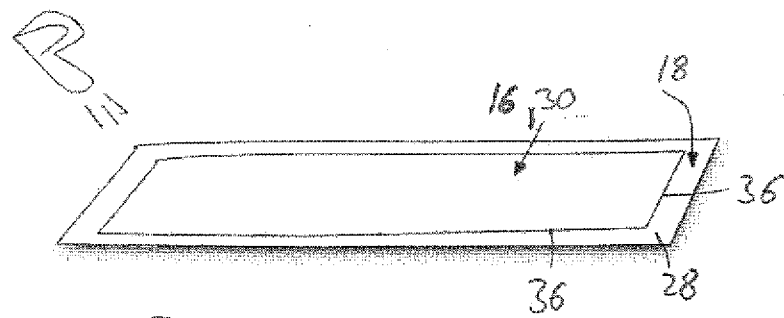


Fig. 5

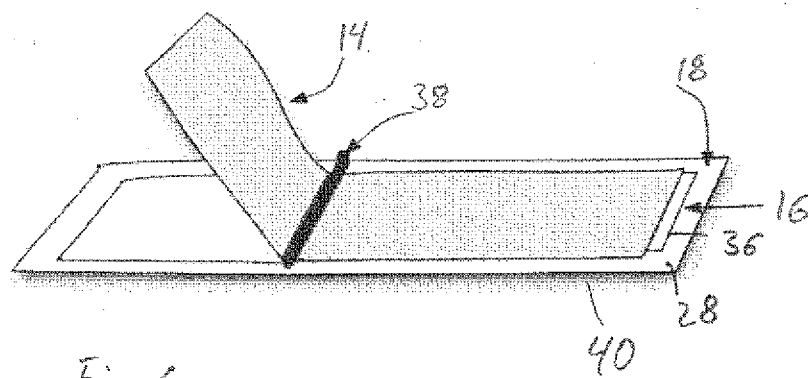


Fig. 6

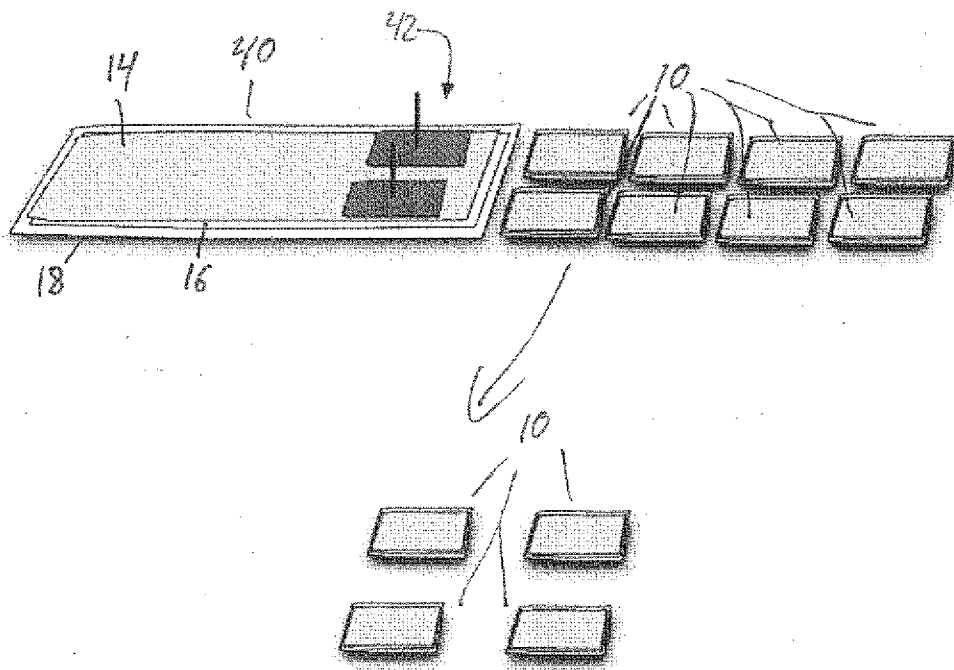


Fig. 7

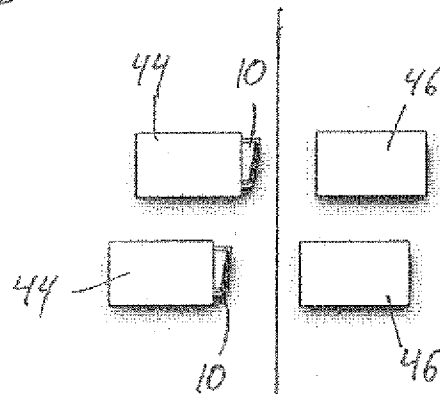


Fig. 8

Fig. 9

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/076584

A. CLASSIFICATION OF SUBJECT MATTER		
INV.	A61K36/8962 A61L15/44	A61K9/00 A61L15/58
	A61K47/32	A61K9/70
		A61L15/24
ADD.		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols) A61K A61L		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, WPI Data, BIOSIS, EMBASE, INSPEC		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2010/247689 A1 (PASPALEEVA-KUEHN VALENTINA [DE] ET AL) 30 September 2010 (2010-09-30) paragraphs [0003], [0023] - [0024], [0139] - [0141] claims 1-27	1-18
Y	US 2006/127437 A1 (KENNEDY JOHN P [US] ET AL) 15 June 2006 (2006-06-15) paragraphs [0062], [0152] - [0159] ----- -/--	1-18
☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 17 February 2014		Date of mailing of the international search report 25/02/2014
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Cadamuro, Sergio

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